

1 GATTCCGGCGGGAGAGAAGTCACCTGCCCTGGCTTACTTGAACTGGTTCTCAGGGTGGGAGAGTCGGGGAGATGCG  
 101 AGCTCTATCCTGTGCCCTGGCTCAGGCAAGCCAGGCTTCCGGACTCGGCTGGCTTAATGAGCTCAGGTCTAGGCCAG  
 201 CAGGGGGCACCTGGCTGGACTCGGCTGG  
 301 GCGGGGGCTGAAGGGGAACCAACGACGGCAGAGAGGCACGGGAGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG  
 1 M E Q R P R G C  
 401 GCGGGGTGGGGGGGGCTCCCTGGCTGGCTGG  
 9 A V A A L L V L L G A R A Q G G T R S P R C D C A G D F H K K  
 501 AGATTGGCTCTGTTTGTGCAGAGGCTGCCAGGGGGCACTACCTGAAGGGCCCCTGGCACGGAGGCCCTGGGGGGGG  
 43 I G L F C C R G C P A G H Y L K A P C T E P C G N S T C L V C P Q  
 601 AGACACCTTCTGGCCTGGGAGAACCATATAATTCTGAATGTCAGGGCCTGTGATGAGCAGGGCCTCCAGGGGGGGGG  
 76 D T F L A W E N H N S E C A R C O A C D E Q A S Q V A L E N C S  
 701 GCAGTGGCGACACCCGCTGTGGCTGTAAGCCAGGGCTACTGTCAGCAGGTCAAGCCAAATGTCAGCAGTTCACCC  
 109 A V A D T R C G C K P G W F V E C Q V S Q C V S P F Y C Q P C L  
 801 TAGACTGGGGCCCTGGCACCACACACGGCTACTCTGTCCCCAGAGATACTGACTGGGACCTGACTGGCTGGCT  
 143 D C G A L H R T R L C S R R D T C G T C L P G F Y E H G D G  
 901 CTGGTGTGCCCTGGGATGGGATGGGATGGGAGGGAGGGGGCTGGGGCTGGGGCTGGGGCTGGGGCTGGGGCTGG  
 176 C V S C P T  
 1001 CAGGAATAGGAAGAGGGATAGGGAGGGAGCCCTGGCCCTGTGATGGGGGGGGGGGGGGGGGGGGGGGGGGGG  
 1101 GCCTTAGCAGATAACATAAGGGTATTGCCCTCACTTCAAGCCAGGATCCTAGCCAGATATTACAGATGATTGTC  
 1201 GAGTCACATTGATATAAGCTTAAACTGGCTGAGGGTTGAGCTATGATCGTGGCAGTGCACCTCAGCCTGGCA  
 1301 ACCTTAAATA  
 1401 TAGTTCTAGGGATCTGGCAAAGTGGAGAATT

**FIG. 1**

**FIG. 2A**

hapo2LI	34	D C A G D - - - F H K K I G L F C C R G C P A G H Y L K A P C T E P C G N S T C L - - - - -
hTNFR1	43	V C P Q G K - - Y I H P Q N N S I C C T K C H K G T Y L Y N D C P G P G Q D T D C R - - - - -
hTNFR2	39	T C R L R E - - Y Y D Q T A Q M C C S K C S P G Q H A K V F C T K T - S D T V C D - - - - -
hTNFRP	42	T C R D Q E K E - Y Y E P Q H R I C C S R C P P G T Y V S A K C S R I - R D T V C A - - - - -
hFAS/Apo1	48	N L E G L - - - H H D G Q F C H K P C P P G E R K A R D C T V N G D E P D C V - - - - -
hLNGFR	31	A C P T G - - - L Y T H S G E C C K A C N L G E G V A Q P C G A - - N Q T V C E - - - - -
hCD40	25	A C R E K - - - Q Y L I N S Q C C S L C O P G Q K L V S D C T E F - T E T E C L - - - - -
hCD27	26	S C P E R - - - H Y W A Q G K L C C Q M C E P G T F L V K D C D Q H R K A A Q C D - - - - -
hCD30	28	T C H G N P S H - Y Y D K A V R R C C Y R C P M G L F P T Q Q C P Q R - - P T D C R K - - - - -
hOX40	30	H C V G D T - - - Y P S N D R C C H E C R P G N G M V S R C S R S - Q N T V C R - - - - -
hapo2LI	72	V C P Q D - T F F L A W E N H H S E C A R C - Q A C D E Q A S O V A L E N C S A V A D T R C G - - - - -
hTNFR1	83	E C E S G - S F T A S E N H L R H C L S C - S K C R K E M G Q V E I S S C T V D R D T V C G - - - - -
hTNFR2	77	S C E D S T Y T Q L W N W V - P E C L S C G S R C S S - - D Q V E T Q A C T R E Q N R I C T - - - - -
hTNFRP	82	T C A E N S Y N E H W N Y L - T I C Q L C - R P C D P V M G L E E I A P C T S K R K T Q C R - - - - -
hFAS/Apo1	84	P C Q E G K E Y T D K A H F S S K C R R C - R L C D E G H G L E V E I N C T R T Q N T K C R - - - - -
hLNGFR	66	P C L D S V T F S D V V S A T E P C K P C - T E C V G L - - Q S M S A P C V E A D D A V C R - - - - -
hCD40	61	P C G E S E F L D T W N R E - T H C H Q H - K Y C D P N L G L R V Q Q K G T S E T D T I C T - - - - -
hCD27	64	P C I P G V S F S S P D H H T R P H C E S C - R H C N S G L L V R - - N C T I T A N A E C A - - - - -
hCD30	68	Q C E P D - Y Y L D E A D R - - C T A C - V T C S R D D L V E K T - P C A W N S S R V C E - - - - -
hOX40	66	P C G P G - F Y N D V V S S K P - C K P C - T W C N L R S G S E R K Q L C T A T Q D T V C R - - - - -

**FIG. 2B**

hAPO2LI	116	C K P G W F V E C Q V S Q C V S S S P F Y C	Q P C L D C G A L H R H T R L L C S R R D - T D C G - T
hTNFR1	127	C R K N Q Y R H Y W S E N L - - -	F Q C F N C S L C L N G - - T V H L S C Q E K Q N T V C - - T
hTNFR2	120	C R P G W Y C A L S K Q E G C - - -	R L C A P L R K C R P G - F G V A R P G T E T S D V V C K - P
hTNFRP	126	C Q P G M F C A A W A L E C - - -	T H C E L L S D C P P G T E A E L K D E V G K G N N H C V - P
hFAS/Apol	129	C K P N F F - - C N S T V C - - -	E H C D P C T K C E H G I - - I K E C T L T S N T K C K -
hLNGFR	109	C A Y G Y Y Q D E T T - - -	G R C E A C R V C E A G S G L - V F S C Q D K Q N T V C E - E
hCD40	105	C E E G W H C T S E A C - - -	E S C V L H R S C S P G F G - V K Q I A T G V S D T I C E - P
hCD27	106	C R N G W Q C R D K E C - - -	T E C D P L P N P S L T A R S S Q A L S P H P Q P T H L P -
hCD30	108	- C R P G M F C S T S A V N S C - - -	A R C F F H S V C P A G M I V K F P G T A Q K - N T V C E -
hOX40	109	- C R A G T Q P L D S Y K P G - - -	V D C A - - -
			- - -
hAPO2LI	164	C L P G F Y E H G D - - -	G C V S C P T
hTNFR1	168	C H A G F F L R E N - - -	E C V S C S N C K K - - - S L E C T K - - - - L C L
hTNFR2	164	C A P G T F S N T T S S T D I C R P H Q I C N V V A I P G N A S M - - -	- D A V C T
hTNFRP	170	C K A G H F Q N T S S P S A R C Q P H T R C E N Q G L V E A A P G T A Q S D T T C K	
hLNGFR	149	C P D G T Y S D E A N H V D P C L P C T V C E D T E R Q L R E C T R W - A D A E C E	
hCD40	146	C P V G F F S N V S S A F E K C H P W T S C E T K D L V V Q Q A G T N K T D V V C G	
hOX40	127	P C P P G H F S P G D - - N Q A C K P W T N C T L Q P A S N S S D A I C E	

1 CGGGCCCTGC GGGGGGGG CTGAAGGG AACACGACG GGCAGAGGC ACGGAGCC  
 61 GAAGCCCTG GGGCCCCGTC GGAGGGCTAT GGAGGAGGG CCCGGGGCT GGGGGGGT  
 112 M F O R P R G C A A V  
 121 GGGGGGGG CTCCTCCTGG TCTCTCTGG GGCCCCGGG CAGGGGGCA CTCGTAGCCC  
 122 A A L L V L L G A R A Q G G T R S P  
 181 CACGTGAC TGTGGGGTG ACTTCACAA GAAGATTGGT CTGTTTGTG GCAGAGGGCTG  
 32 R C D C A G D F H K K I G L F C C R G C  
 321 CCCAGGGG CACTACCTGA AGGCCCTTG CACGGAGCCC TGGGGAACT CCACCTGCT  
 52 P A G H Y L K A P C T E P C G N S T C L \*  
 301 TGTGTCCC CAAGACACCT TCTGGCTTG GGAGAACAC CATAATTCTG AATGTGGCC  
 72 V C P Q D T F L A W E N H H N S E C A R  
 361 CTGCGGGC TGTGATGAC AGGCCTCCA GTGGGGCTG GAGAATGTT CAGCAGTGGC  
 92 C Q A C D E Q A S Q V A L E N C S A V A \*  
 421 CGACACCCGC TGTGGCTTA AGCCAGGCTG GTTGTGGAG TGCCAGGTCA GCCAATGCT  
 112 D T R C G C K P G W F V E C Q V S Q C V  
 481 CAGCACTTCA CCCTTCTACT GCAAACCATG CCTAGACTGC GGGGCCCTGC ACCGCCAC  
 132 S S S P F Y C Q P C L D C G A L H R H T

FIG. 4A

## FIG. 4B

541 ACGGCTACTC TGTCCCCGA GAGATACTCA CTGGGGGACCA CGCCCTGCCCTG GCCTCTATGA  
152 R L L C S R R D T D C G T C L P G F Y E

601 ACATGGCGAT GGCTGGCTGT CCTGGCCCCAC GAGCACCCCTG GGGAGCTGTC CAGAGGGCTG  
172 H G D C V S C P T S T L G S C P E R C

661 TGCCGGCTGTC TGTGGCTGCA GGCAGATGTT CTCGGTCCAG GTGCTCCCTGG CTGGCCCTGT  
192 A A V C G W R Q M F W Y O V L H A G L Y

721 GGTCCCCCTC CTGCTTGCGG CCACCCCTGAC CTACACATAC CGCCACACTGGT GGCCTCACAA  
212 Y P L L L G A T L T Y T X R H C W P H K

781 GCCCCCTGGTT ACTGGAGATG AACCTGGAT GGAGGCTCTG ACCCCACCCAC CGGCCACCCA  
232 P L V T [A] D E A G W E A L T P P P A T H

841 TCTCTCACCC TTGGACAGCC CCCAACCCCT TCTAGGACACT CCTGACACCA GTGAGAAGAT  
252 L S P L D S A H T L L A P P D S S E K I

901 CTGGCACCGTC CAGTTGGTGG GTAACAGCTG GACCCCTGGC TACCCCGAGA CCCAGGGCC  
272 C T V Q L V G N S W T P G Y P E T Q E A

961 GCTCTGCCCG CAGGTGACAT GGTCCCTGGGA CCAAGTGGCC AGCAGAGCTC TTGGCCCCGGC  
292 L C P Q V T W S W D Q L P S R A L G P A

1021 TGCTGGCCC ACACCTCTCGC CAGAGTCCCC AGCCGGCTCG CCAGCCATGA TGCTGGAGCC  
312 A A P T L S P E S P A G S P A M M L Q P

1081 GGCCTGGAG CTCTACGACG TGATGGACCC GCTCCCCAGCG CGGGGCTGGA AGGAGCTTCGT  
 332 G P Q L Y D V M D A V P A R R W K E F V

1141 GCGCACCCCTTC GGGCTGGCC AGGAGAGAT CGAAGCCCTG GACCTGGAGA TCGCCCCCTT  
 352 R T L G L R E A E I F A V E V F I G R F V

1201 CCGAGACCCAG CACTAACGACA TCGCTCAAGCG CTGGCCCCAG CACCAAGCCCG CGGGCCTCG  
 372 R D Q Q Y E M L K R W R Q Q P A G L G

1261 AGCCCGTTAC CGGGCCCTTG AGCCCATGGC GCTGGACGGC TGGCTGGAG ACTTCGCCAG  
 392 A V Y A A L E R M G L D G C V F D L R S

1321 CCGCCCTGGAG CGGGCCCTGT GACACGGCC CGACTTGCCA CCTAGCCCT CTGGTGGCC  
 412 R L Q R G P

1381 TTGCAAGAC CCTAAAGTACG GTTACTTATG CGTCTAGACA TTTATGTC A CTATTAGC

1441 CGCTGGCAG GCCCTGGCTA CGAGCACCAG CGGGCCAC CCCTGCTGC CCCTATCGT

1501 CCAGCCAAGG CGAAGAAGCA CGAACGAATG TCGAGAGGG GTGAAGACAT TTCTCAACTT

1561 CTCGGCCCGA GTTTCGGCTA GATCGCCGTA TTAATCTGT GAAGAAGAC AAAAAMAA

1621 AAAAAMAA AAAA

FIG. 4C

**FIG. 5**

Apo3	1	M E O R P R G C A A V A A A L L L V L I I G A R A Q G G T R S P R - - - - -
TNFR1	1	M G L S T V P D I L L P L L - V L L E L L V G I Y P S G V I G L V P H L G D R E K R D S V
Fas/Apo1	1	M L G I W T L L P L V L T S V A R L S S K S V N A Q V T D I N S K G L E L R K T V T V
Apo3	3 3	C D C A G D F H K K I G L F C C R G C P A G H Y L K A P C T E P C G N S T C L V
TNFR1	4 4	C P Q G K Y I H P Q N N S I C C T K C H K G T Y L Y N D C P G P G Q D T P C R E
Fas/Apo1	4 5	E T Q N I L E G L H H D G Q E C H K P C P P G E R K A R D C T V N G D E P D C V P
Apo3	7 3	C P Q D T F L A W E N H H N S E C A E C Q A C D E Q A S Q V A L E N C S A V A D T R C G
TNFR1	8 5	C E S G S E T T A S E N H L R H - C L S C S K C R K E M G Q V E I S S C T V D R D T V C G
Fas/Apo1	8 5	C Q E G K E Y T D K A H F S S K C R R C R L C D E G H G L E V E I N C T R T Q N T K C R
Apo3	1 1 7	C K P G W F V E C Q V S Q C V S S S P F Y C Q P C L D C G A L H R H T R L L C S R R D - T D C G T
TNFR1	1 2 7	C B K N Q Y R H Y W S E N L F Q - - - - C F N C S L C L N G T V E I L S - - C Q E K Q N T V C T -
Fas/Apo1	1 2 9	C K P N F F - - C N S T V C E H - - - - C D P C T K C E H G I I K E - - - C T L T S N T K C K E
Apo3	1 6 5	C L P G F Y E H G D G C V S C P T S T L G S C P - - E R C A A V C G W
TNFR1	1 6 8	C H A G F F L R E N E C V S C S - - - - N C K K S L E C T K L C L P

1995 2000 2005 2010 2015 2020 2025 2030 2035

Apo3	3 3 8	V M D A V P A R R W K E F V R T I G R E A E T E A V E I G R - - F R D Q Q Y E
TNFR1	3 3 3	V V E N V P P L R W K E F V R R L G S D H E I D R L E L Q N G R - C L R E A Q Y S
Fas/Apo1	2 2 0	I A G V M T I L S Q V K G F V R K N G V N E A K I D E I K N D N V Q D T A E Q K V - Q
FADD	1 0 4	I C D N V G K - D W R R L A R Q L K V S D T K I D S I E D R Y P R N - L T E V R E
TRADD	2 1 1	N R P I S L K - D Q Q T F E A R S V G L K W R K V G R - S L Q R G C R A I R D P A L D
RIP	2 9 1	I R E N I G K - H W K N C A R K L G F T Q S A I D E I D H D Y E R D G L K E K V Y Q
Reaper	1	M A V A F Y I P D Q A T L L R E A E Q K E Q Q I I R - L R E S Q W R
Apo3	3 7 8	M L K R W R Q Q P - - - A G L G A V Y A A L E R M G I - D G C V E D L R S
TNFR1	3 7 4	M L A T W R R R T P R R E A T I E L L G R V L R D M D I L - L G C L E D I E E
Fas/Apo1	2 6 1	I L L R N W H O L H G - K K E A Y D T L I K D L K K A N L C T L A - E K I Q T
FADD	1 4 4	S L R I N K N T E - K E N A T V A H L V G A L R S C - - - Q M N E V A D L V
TRADD	2 5 1	S L A Y E Y E E G L Y E Q A F Q L L A R E F V - Q A E G R A T I O R L V E
RIP	3 3 2	M L Q N W V M R E G I K G A T V G K L A Q A L H Q C - - S R I D E L S S L T
Reaper	3 4	F L A T V V L E T L K Q Y T S C H P K T G R K S G K Y R K P

FIG. 6

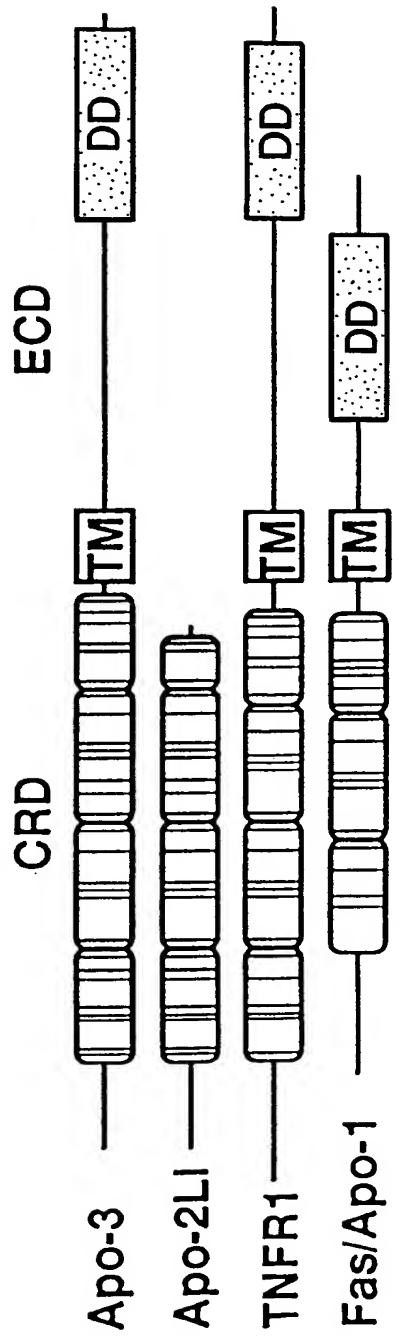
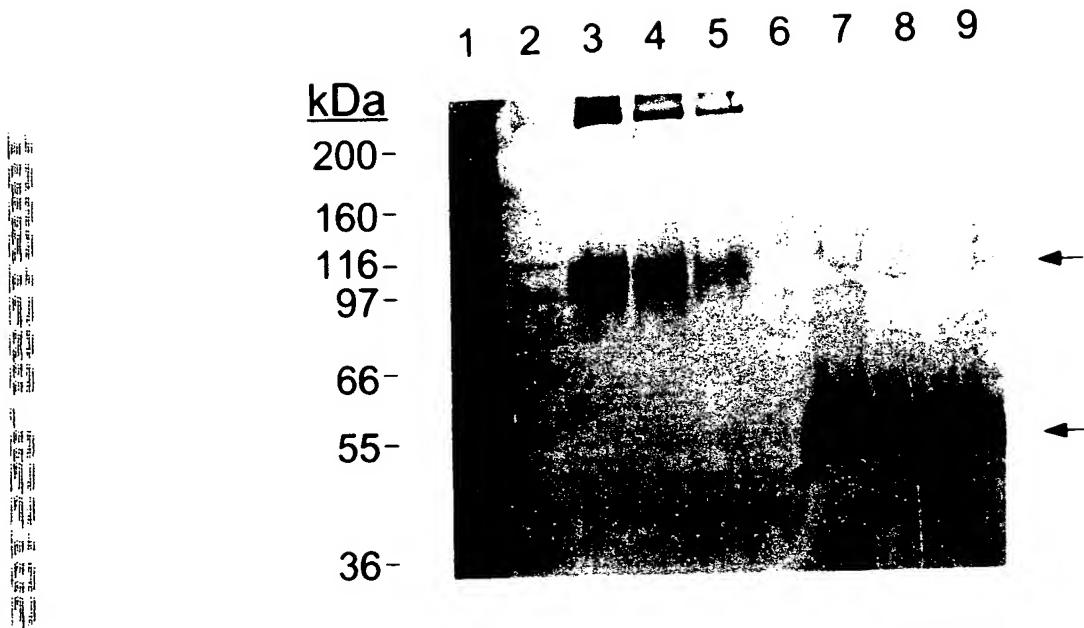


FIG. 7



**FIG. 3**

1 2 3

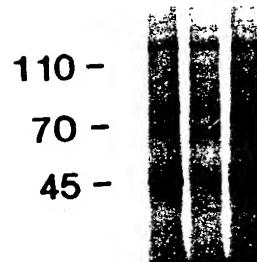


FIG. 8

1 2 3 4 5 6 7 8 9

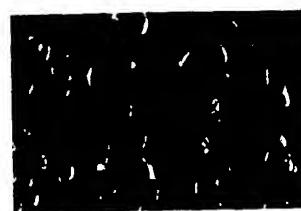


FIG. 10

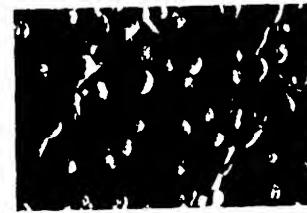
**FIG. 9A**



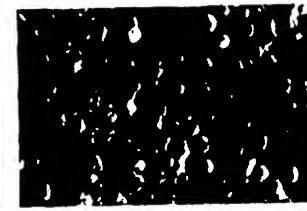
**FIG. 9C**



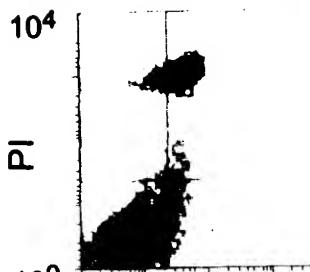
**FIG. 9B**



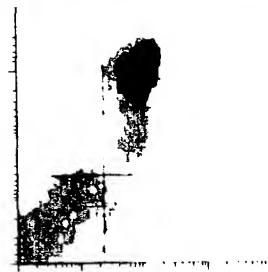
**FIG. 9D**



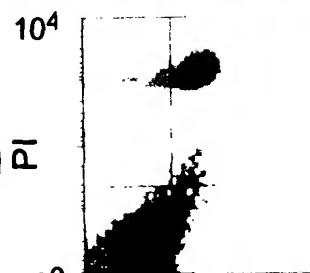
**FIG. 9E**



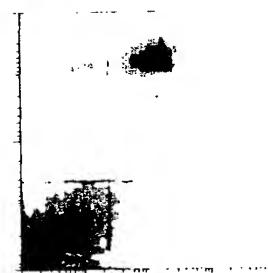
**FIG. 9F**



**FIG. 9G**

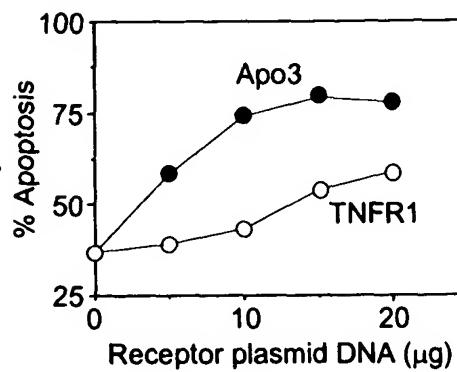


**FIG. 9H**



Annexin-V-FITC

**FIG. 9I**



1 2 3 4

**FIG. 9J**

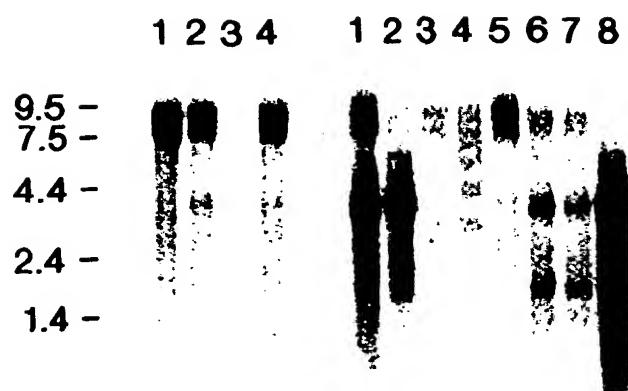


**Transfection**

**pRK5**  
**TNFR1**  
**Apo-3**

— Phospho-C-Jun

**FIG. 11**



**FIG. 12**